Lung Cancer UPDATES
ESMO HIGHLIGTHS
20-24 OCTUBRE 2023
Madrid, Spain

Iniciativa científica de:
GECP
lung cancer research

Enfermedad Metastática con alteraciones driver: EGFR

Oscar Juan Vidal

Hospital Univesitari i Politècnic La Fe

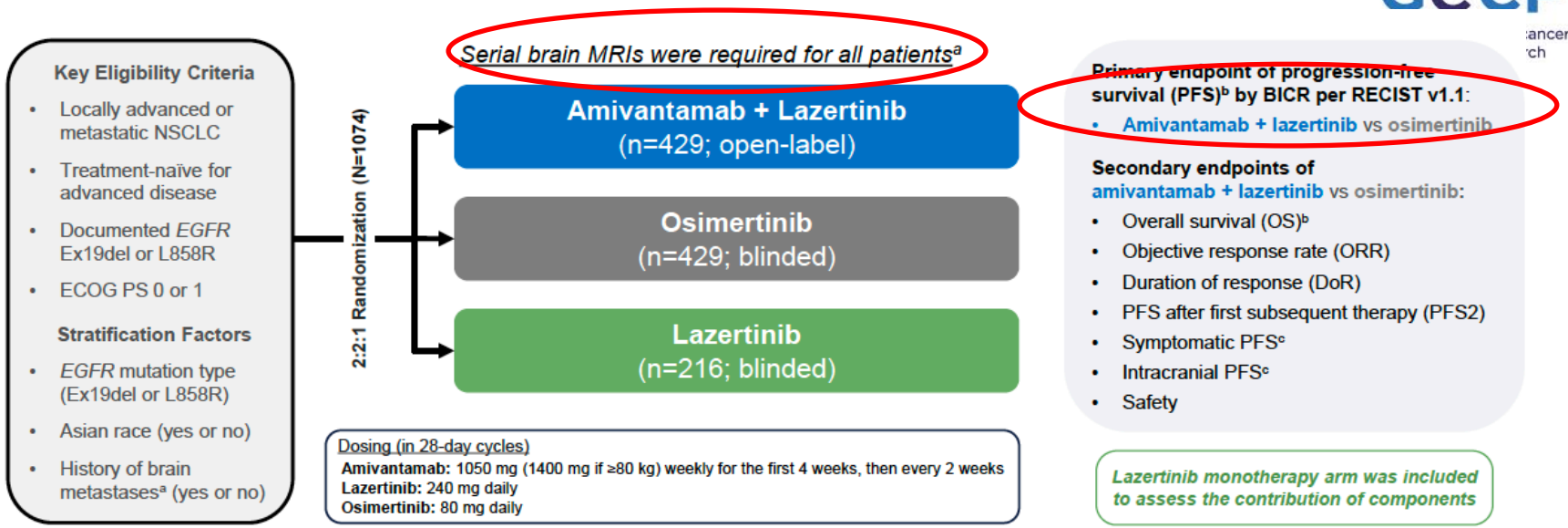
Primera línea en paciente EGFRm

MARIPOSA

Amivantamab Plus Lazertinib Versus Osimertinib as First-line Treatment in *EGFR*-mutated Advanced NSCLC

Primary Results from MARIPOSA, a Phase 3, Global, Randomized, Controlled Trial

Byoung Chul Cho,[1] Enriqueta Felip,[2] Alexander I. Spira,[3] Nicolas Girard,[4] Jong-Seok Lee,[5] Se-Hoon Lee,[6] Yuriy Ostapenko,[7] Pongwut Danchaivijitr,[8] Baogang Liu,[9] Adlinda Alip,[10] Ernesto Korbenfeld,[11] Josiane Mourão,[12] Tao Sun,[13] Melissa Martinez,[13] Joshua M. Bauml,[14] S. Martin Shreeve,[15] Seema Sethi,[14] Roland E. Knoblauch,[14] Hidetoshi Hayashi,[16] Shun Lu[17]

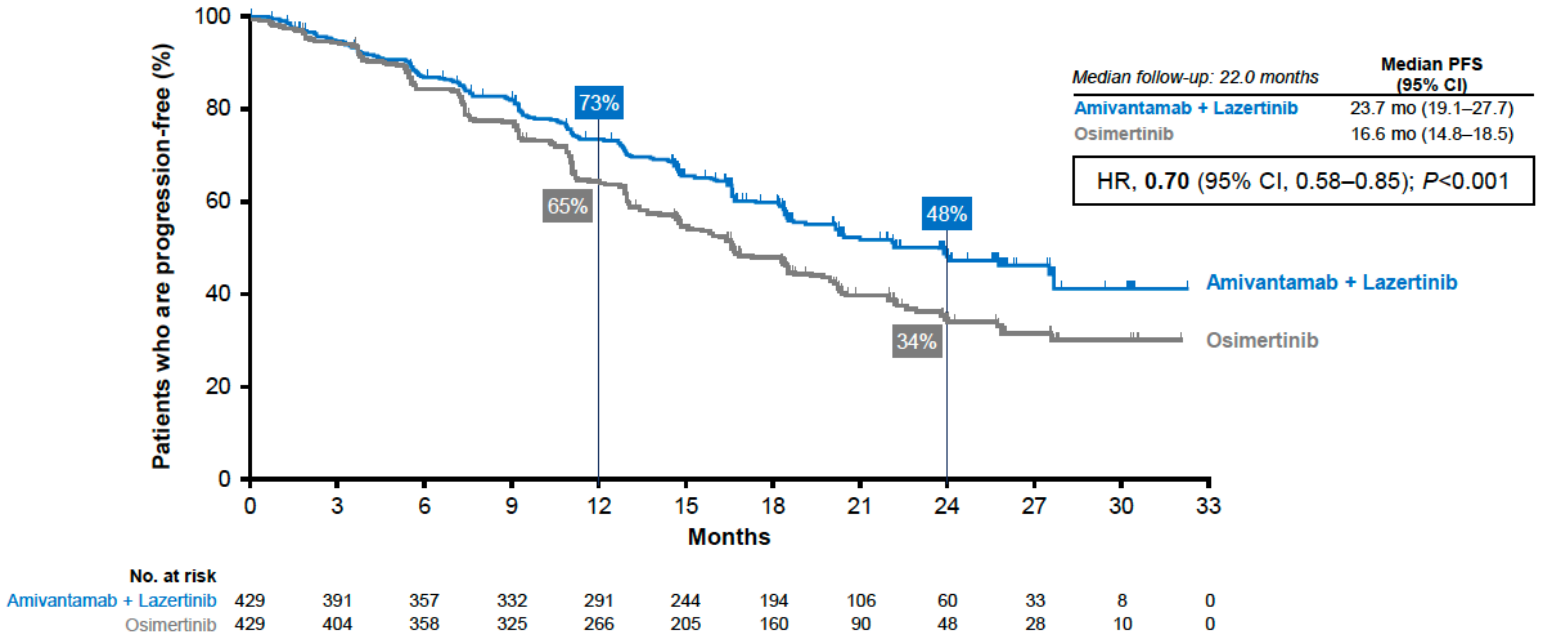


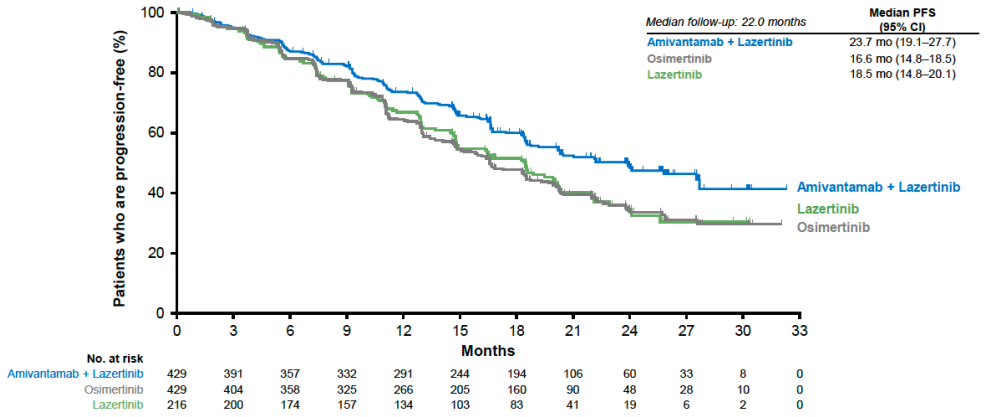
Characteristic, n (%)	Amivantamab + Lazertinib (n=429)	Osimertinib (n=429)	Lazertinib (n=216)
Median age, years (range)	64 (25-88)	63 (28-88)	63 (31-87)
Female	275 (64)	251 (59)	136 (63)
Race			
Asian	250 (58)	251 (59)	128 (59)
White	164 (38)	165 (38)	79 (37)
Other[a]	15 (3)	13 (3)	9 (4)
ECOG PS 1	288 (67)	280 (65)	140 (65)
History of smoking	130 (30)	134 (31)	73 (34)
History of brain metastases	178 (41)	172 (40)	86 (40)
EGFR mutation type[b]			
Ex19del	258 (60)	257 (60)	131 (61)
L858R	172 (40)	172 (40)	85 (39)
Adenocarcinoma subtype	417 (97)	415 (97)	212 (98)

Primera línea en paciente EGFRm

MARIPOSA

Primary Endpoint: PFS by BICR





Amivantamab + Lazertinib reduce en un 30% el riesgo de progression y aumenta en 7 meses la mPFS: 23.7 vs 16.6 m

Lazertinib mostró similar eficacia al osimertinib

Primera línea en paciente EGFRm

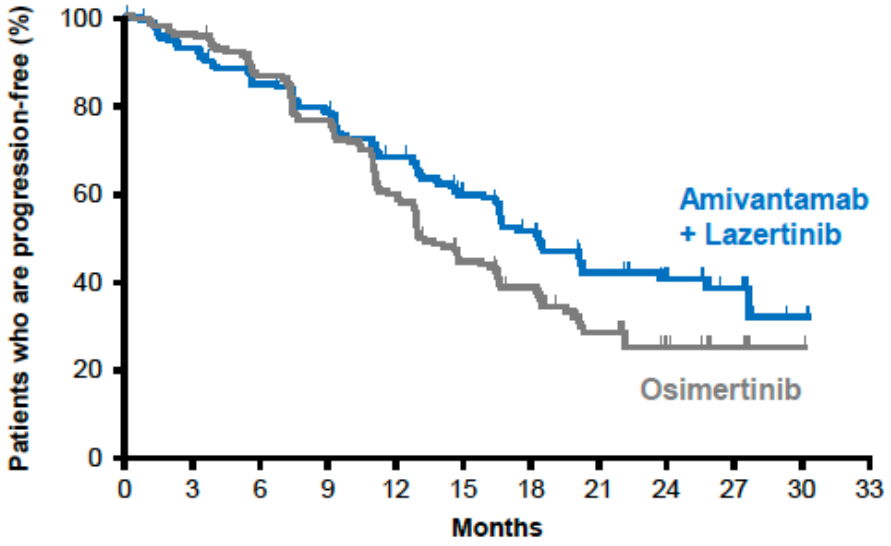
MARIPOSA

Iniciativa científica de: GECP lung cancer research

Beneficio similar en pacientes con y sin MTS cerebrales

With History of Brain Metastases	Median PFS (95% CI)
Amivantamab + Lazertinib	18.3 mo (16.6–23.7)
Osimertinib	13.0 mo (12.2–16.4)

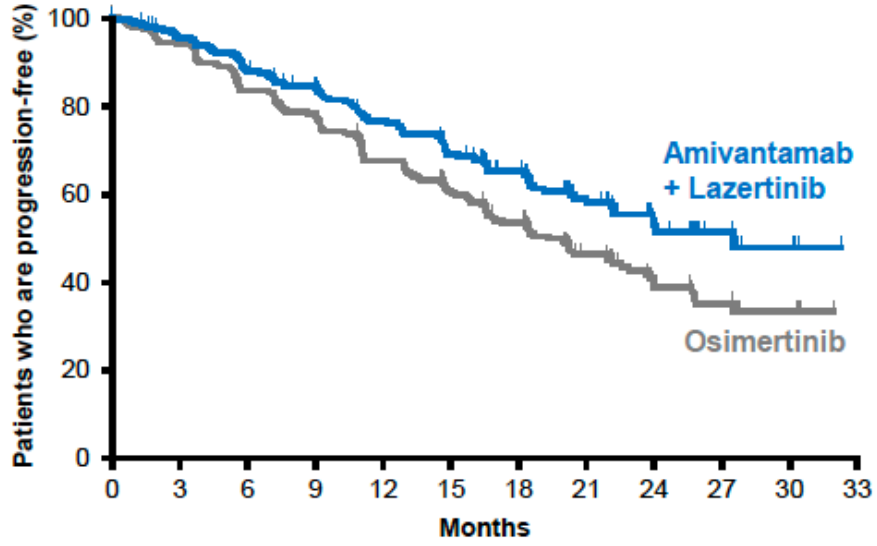
HR, **0.69** (95% CI, 0.53–0.92)



No. at risk												
Amivantamab + Lazertinib	178	162	146	134	115	92	71	34	24	12	3	0
Osimertinib	172	164	146	126	95	64	47	21	11	6	1	0

Without History of Brain Metastases	Median PFS (95% CI)
Amivantamab + Lazertinib	27.5 mo (22.1–NE)
Osimertinib	19.9 mo (16.6–22.9)

HR, **0.69** (95% CI, 0.53–0.89)



No. at risk												
Amivantamab + Lazertinib	251	229	211	198	176	152	123	72	36	21	5	0
Osimertinib	257	240	212	199	171	141	113	69	37	22	9	0

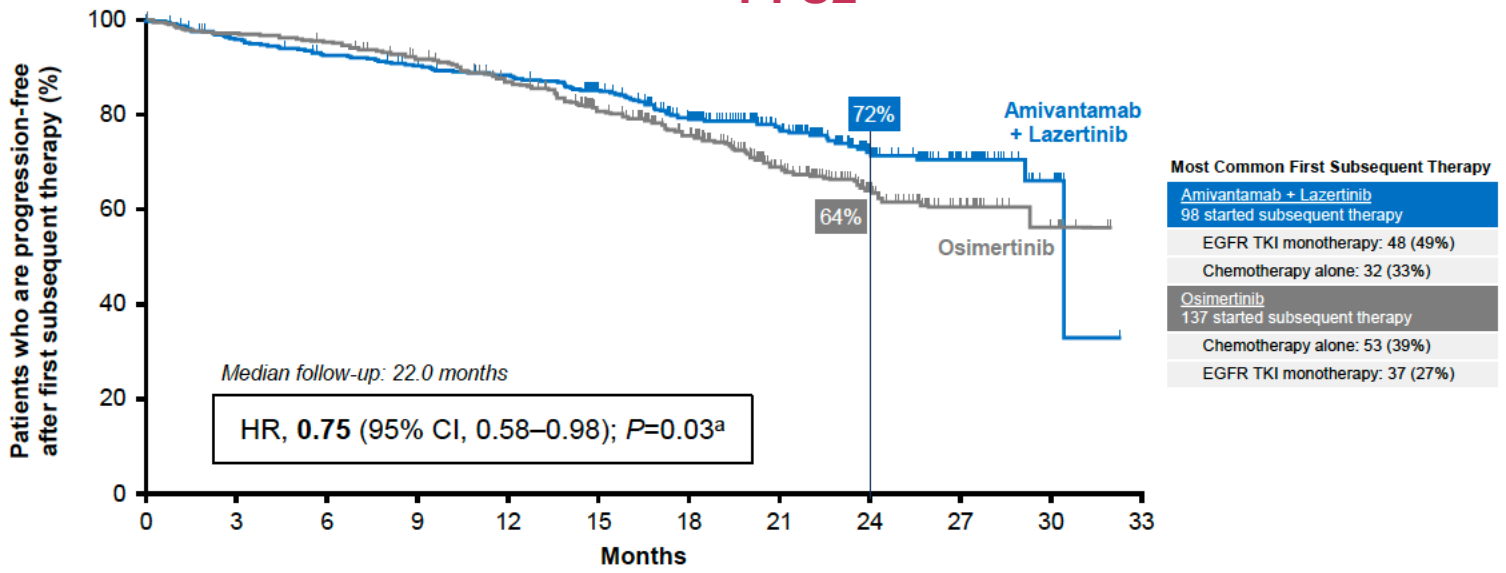
Primera línea en paciente EGFRm

MARIPOSA

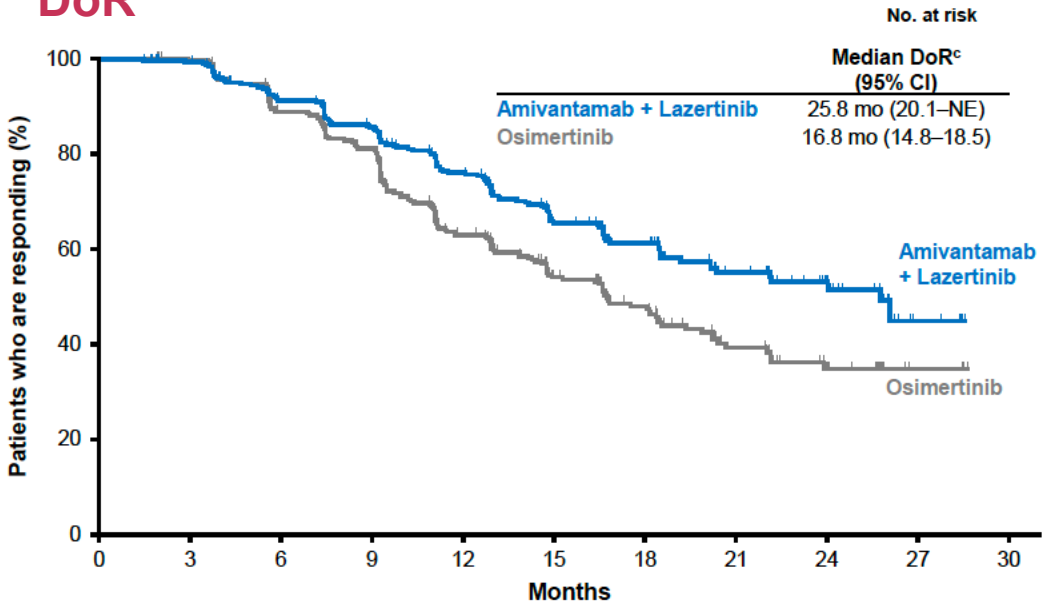
ORR

BICR-assessed response, n (%)[a]	Amivantamab + Lazertinib (n=429)	Osimertinib (n=429)
ORR		
All responders	86% (95% CI, 83–89)	85% (95% CI, 81–88)
Confirmed responders	80% (95% CI, 76–84)	76% (95% CI, 71–80)
Best response[b]		
CR	29 (7)	15 (4)
PR	334 (79)	335 (81)
SD	30 (7)	42 (10)
PD	7 (2)	11 (3)
NE/UNK	21 (5)	11 (3)
Ongoing responses	209 of 336 (62%)	151 of 314 (48%)

PFS2



DoR



Ami+Lazer reduce el riesgo de la 2ª progression en un 25%

Datos de OS inmaduros, no diferencias significativas

Primera línea en paciente EGFRm

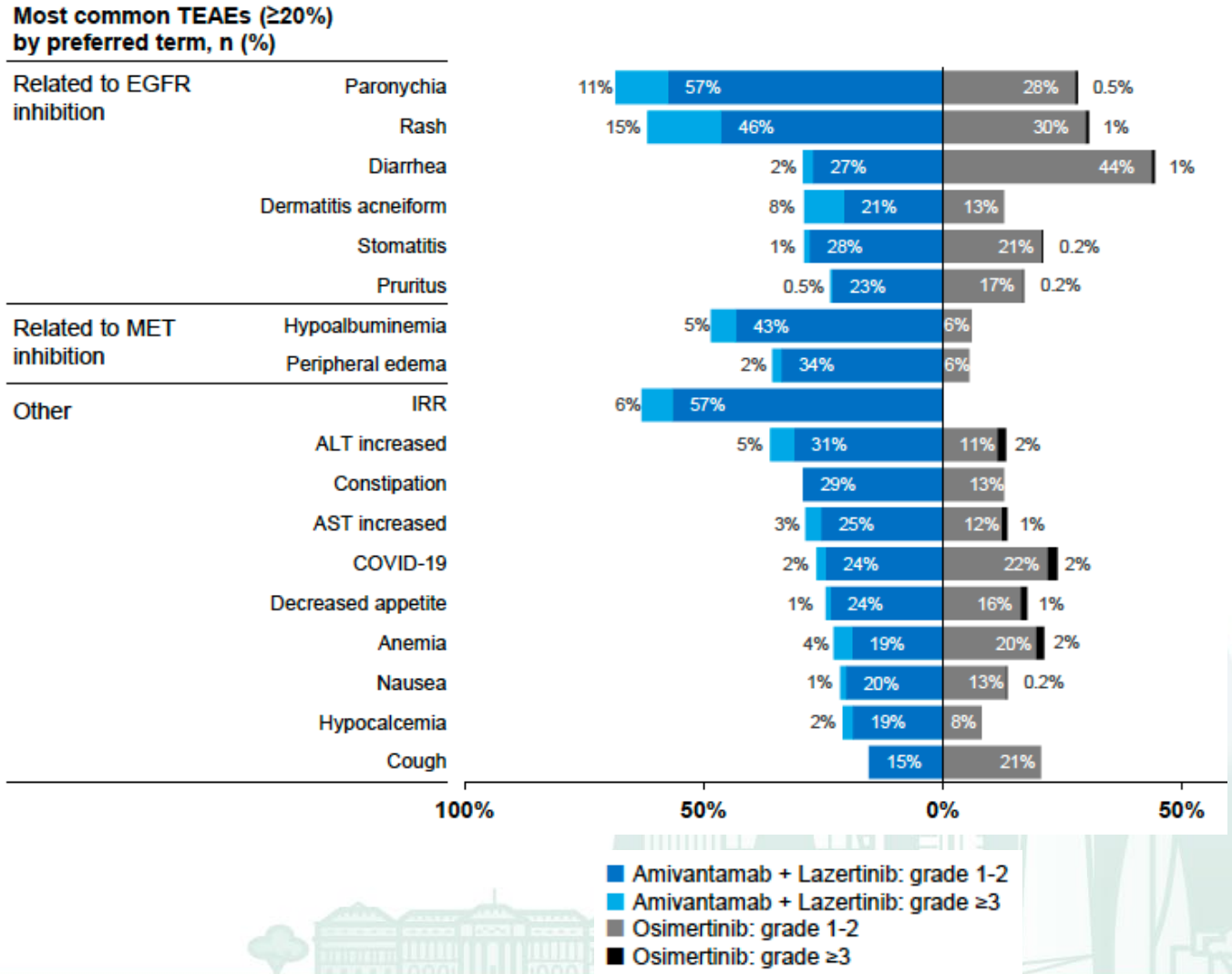
MARIPOSA: Efectos adversos

Iniciativa científica de: GECP lung cancer research

TEAE, n (%)	Amivantamab + Lazertinib (n=421)	Osimertinib (n=428)
Any AE	421 (100)	425 (99)
Grade ≥3 AEs	316 (75)	183 (43)
Serious AEs	205 (49)	143 (33)
AEs leading to death	34 (8)	31 (7)
Any AE leading to treatment:		
Interruptions of any agent	350 (83)	165 (39)
Reductions of any agent	249 (59)	23 (5)
Discontinuations of any agent	147 (35)	58 (14)

Treatment-related AEs leading to discontinuations of all agents occurred in 10% of patients treated with amivantamab + lazertinib and 3% with osimertinib

VTE 37% vs 9%
La mayoría grado 1-2
Discontinuación 3% vs 0.5%
Inicio más temprano



2ª línea en pacientes EGFRm. Progresión a osimertininb

Ensayo MARIPOSA 2

Iniciativa científica de: GECP lung cancer research

Amivantamab Plus Chemotherapy (With or Without Lazertinib) vs Chemotherapy in *EGFR*-mutated, Advanced NSCLC After Progression on Osimertinib

MARIPOSA-2, a Phase 3, Global, Randomized, Controlled Trial

Antonio Passaro,[1] Byoung Chul Cho,[2] Yongsheng Wang,[3] Barbara Melosky,[4] Raffaele Califano,[5] Se-Hoon Lee,[6] Nicolas Girard,[7] Karen Reckamp,[8] Toshiaki Takahashi,[9] Enriqueta Felip,[10] Ryan D. Gentzler,[11] Sanjay Popat,[12] William Nassib William Jr,[13] Tao Sun,[14] Sujay Shah,[15] Brooke Diorio,[16] Roland E. Knoblauch,[15] Joshua M. Bauml,[15] Rosario Garcia Campelo,[17] Jie Wang[18]

Study Design

Key Eligibility Criteria
- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1
- Stable brain metastases were allowed; radiation/definitive therapy was not required (untreated)

Stratification Factors
- Osimertinib line of therapy (1st vs 2nd)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=657)

Serial brain MRIs were required for all patients[a]

- **Amivantamab-Lazertinib-Chemotherapy (n=263)**
- **Chemotherapy (n=263)**
- **Amivantamab-Chemotherapy (n=131)**

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at Cycle 3 (week 7)

Lazertinib: 240 mg daily starting after completion of carboplatin[b]

Chemotherapy administered at the beginning of every cycle:
- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m² until disease progression

Dual primary endpoint of PFS[c] by BICR per RECIST v1.1:
- **Amivantamab-Lazertinib-Chemotherapy** vs **Chemotherapy**
- **Amivantamab-Chemotherapy** vs **Chemotherapy**

Secondary endpoints:
- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- Intracranial PFS
- Time to subsequent therapy[d]
- PFS after first subsequent therapy (PFS2)[d]
- Symptomatic PFS[d]
- Safety

Aumento de SAE en el brazo A (Ami+Lazer+Ch) → No empezar Lazer hasta finalizer el carboplatino

Currently ongoing

Same eligibility criteria as the main study

Randomization (N~90)

- ***Modified* Amivantamab-Lazertinib-Chemotherapy (n~60)**
- **Amivantamab-Chemotherapy (n~30)**

Key endpoints[b]:
- Safety
- Progression-free survival (PFS)
- Objective response rate
- Duration of response
- Intracranial PFS

166 p Lazertinib concurente
97p después fin de Carbo

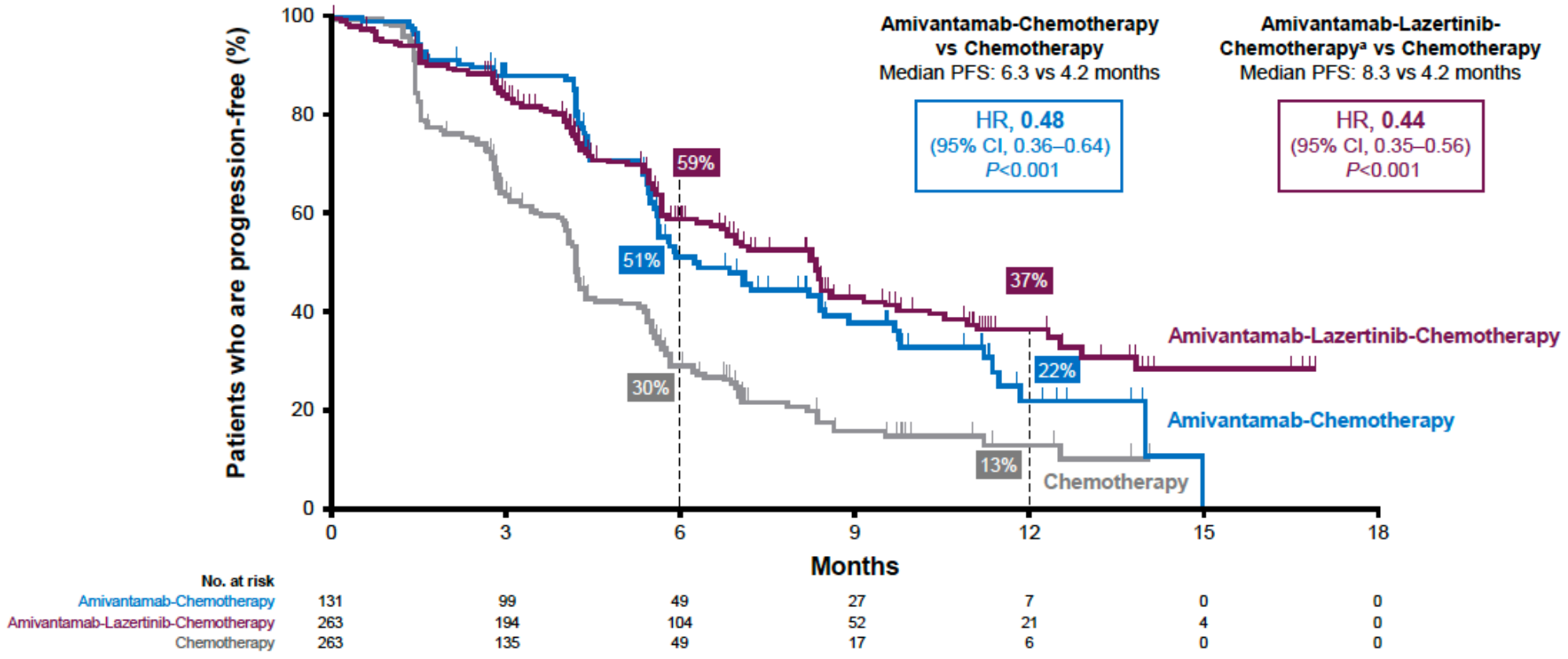
2ª línea en pacientes EGFRm. Progresión a osimertininb

Ensayo MARIPOSA 2: Eficacia

Iniciativa científica de: GECP lung cancer research

- 48% Asian
- 46% Brain Mts
- 70% Osi 1L
- 70% Ex19del

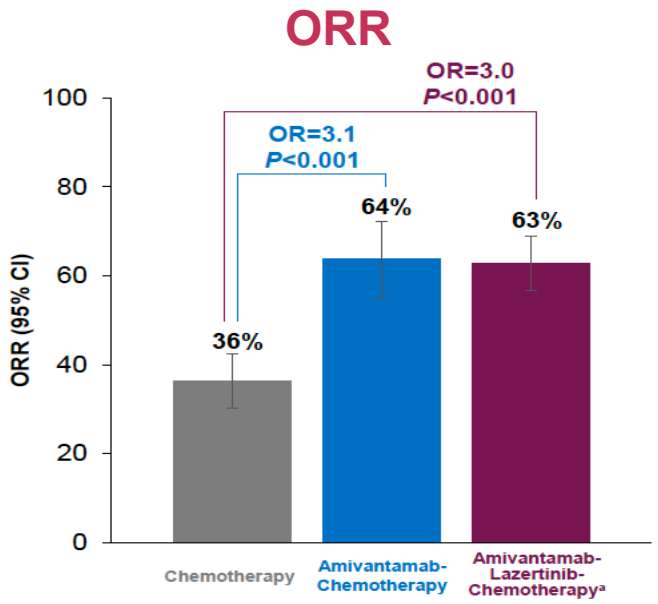
Primary Endpoint: PFS by BICR



Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; *P*<0.001[b]) & HR, 0.38 (8.3 vs 4.2 mo; *P*<0.001[b])

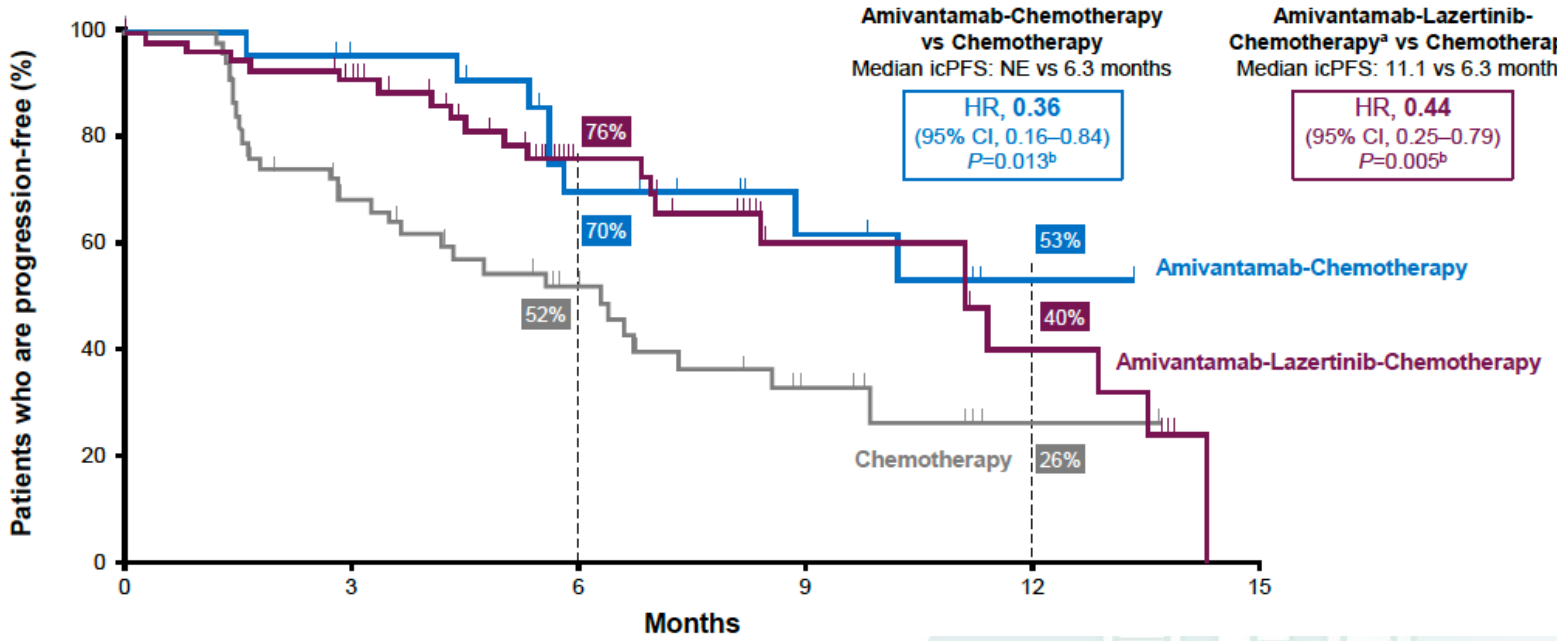
2ª línea en pacientes EGFRm. Progresión a osimertininb

Ensayo MARIPOSA 2: Eficacia



BICR-assessed Response, n (%)[b]	Chemotherapy (n=263)	Amivantamab-Chemotherapy (n=131)	Amivantamab-Lazertinib-Chemotherapy (n=263)
Best Response			
CR	1 (0.4)	2 (2)	6 (2)
PR	93 (36)	81 (62)	157 (61)
SD	82 (32)	30 (23)	61 (24)
PD	52 (20)	10 (8)	14 (5)
NE/UNK	32 (12)	7 (5)	21 (8)
Median DoR[c]	5.6 mo (95% CI, 4.2–9.6)	6.9 mo (95% CI, 5.5–NE)	9.4 mo (95% CI, 6.9–NE)

Intracranial PFS by BICR in patients with and without BM



2ª línea en pacientes EGFRm. Progresión a osimertininb

Ensayo MARIPOSA 2: Efectos Adversos

Iniciativa científica de: GECP lung cancer research

	Chemotherapy (n=243)	Amivantamab-Chemotherapy (n=130)	Amivantamab-Lazertinib-Chemotherapy[a] (n=263)
Treatment duration, median (range)	3.7 months (0–15.9)	6.3 months (0–14.7)	5.7 months (0.1–18.6)
No. of chemotherapy cycles, median (range)			
Carboplatin	4 (1–5)	4 (1–4)	4 (1–4)
Pemetrexed	6 (1–23)	9 (1–22)	7 (1–25)

TEAE, n (%)	Chemotherapy (n=243)	Amivantamab-Chemotherapy (n=130)	Amivantamab-Lazertinib-Chemotherapy[a] (n=263)
Any AEs	227 (93)	130 (100)	263 (100)
Grade ≥3 AEs	117 (48)	94 (72)	242 (92)
Serious AEs	49 (20)	42 (32)	137 (52)
AEs leading to death	3 (1)	3 (2)	14 (5)
Any AE leading to treatment:			
Interruptions of any agent	81 (33)	84 (65)	202 (77)
Reductions of any agent	37 (15)	53 (41)	171 (65)
Discontinuations of any agent	9 (4)	24 (18)	90 (34)
Discontinuations of all agents due to AE	10 (4)	14 (11)	38 (14)

Most common TEAEs (≥25%) by preferred term, n (%)	Chemotherapy (n=243)		Amivantamab-Chemotherapy (n=130)		Amivantamab-Lazertinib-Chemotherapy[a] (n=263)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Associated with EGFR inhibition						
Paronychia	1 (0.4)	0	48 (37)	3 (2)	133 (51)	11 (4)
Rash	12 (5)	0	56 (43)	8 (6)	126 (48)	17 (6)
Stomatitis	21 (9)	0	41 (32)	1 (1)	120 (46)	24 (9)
Diarrhea	16 (7)	1 (0.4)	18 (14)	1 (1)	68 (26)	10 (4)
Associated with MET inhibition						
Hypoalbuminemia	21 (9)	1 (0.4)	29 (22)	3 (2)	104 (40)	12 (5)
Peripheral edema	15 (6)	0	42 (32)	2 (2)	85 (32)	1 (0.4)
Associated with Chemotherapy						
Neutropenia	101 (42)	52 (21)	74 (57)	59 (45)	181 (69)	144 (55)
Thrombocytopenia	72 (30)	22 (9)	57 (44)	19 (15)	158 (60)	96 (37)
Anemia	97 (40)	23 (9)	51 (39)	15 (12)	141 (54)	48 (18)
Leukopenia	68 (28)	23 (9)	37 (28)	26 (20)	106 (40)	71 (27)
Other						
Infusion-related reaction	1 (0.4)	0	76 (58)	7 (5)	148 (56)	9 (3)
Nausea	90 (37)	2 (1)	58 (45)	1 (1)	131 (50)	16 (6)
Constipation	72 (30)	0	50 (38)	1 (1)	96 (37)	3 (1)
Decreased appetite	51 (21)	3 (1)	40 (31)	0	85 (32)	7 (3)
Vomiting	42 (17)	1 (0.4)	32 (25)	1 (1)	76 (29)	10 (4)
Fatigue	47 (19)	4 (2)	36 (28)	4 (3)	69 (26)	15 (6)
Asthenia	40 (16)	5 (2)	34 (26)	1 (1)	67 (25)	14 (5)
Alanine aminotransferase increased	67 (28)	10 (4)	26 (20)	7 (5)	55 (21)	14 (5)
AESIs by grouped term, n (%)						
Rash[b]	30 (12)	0	92 (71)	13 (10)	197 (75)	40 (15)
VTE[c]	11 (5)	7 (3)	13 (10)	3 (2)	58 (22)	17 (6)
ILD	0	0	2 (2)	1 (1)	7 (3)	5 (2)

2ª línea en pacientes EGFRm. Progresión a osimertininb

TROPION-Lung 05

Iniciativa científica de: GECP lung cancer research

TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd) in previously treated non-small cell lung cancer with actionable genomic alterations

Luis Paz-Ares,[1] Myung-Ju Ahn,[2] Aaron Lisberg,[3] Satoru Kitazono,[4] Byoung Chul Cho,[5] George Blumenschein Jr,[6] Elaine Shum, [7] Elvire Pons Tostivint,[8] Yasushi Goto,[9] Kiyotaka Yoh,[10] Rebecca Heist,[11] Paul Baas,[12] David Planchard,[13] Maurice Pérol,[14] Enriqueta Felip,[15] Wu-Chou Su,[16] Hong Zebger-Gong,[17] Lan Lan,[18] Chelsea Liu,[18] Jacob Sands[19]

Diseño: Fase 2

Screening

Key inclusion criteria

- Stage IIIB, IIIC, or IV NSCLC
- Presence of ≥1 actionable genomic alteration (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
- ECOG PS of 0 or 1
- ≥1 line of targeted therapy
- 1 or 2 prior cytotoxic agent–containing therapies including platinum-based therapy in the metastatic setting
- Radiographic disease progression after targeted therapy

Treatment

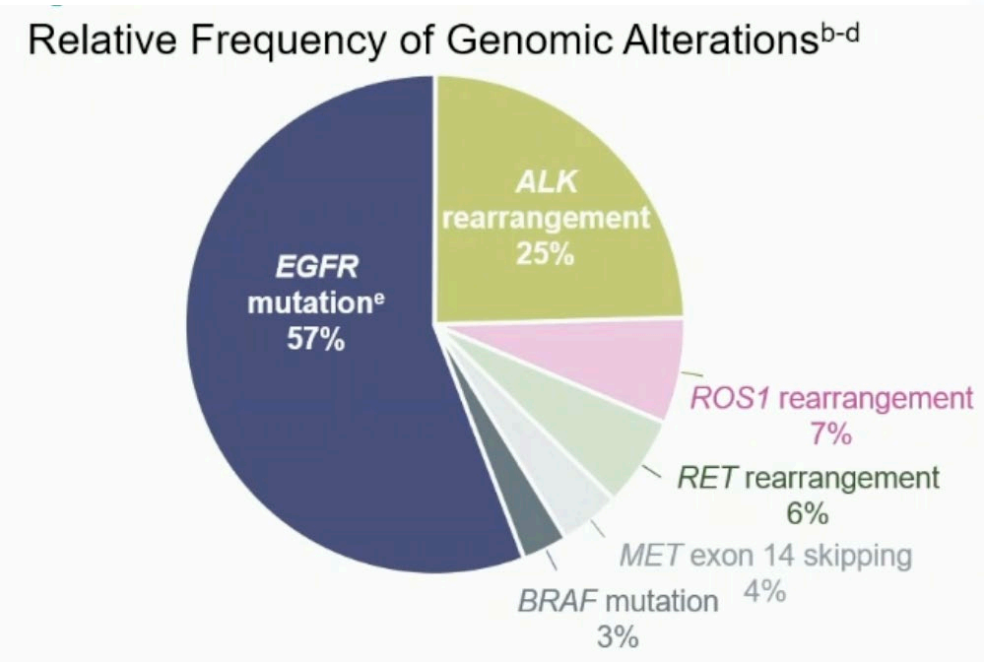
Dato-DXd
6 mg/kg
Q3W

Endpoints[a]

Primary: ORR by BICR
Secondary:

- By BICR and investigator: DOR, DCR, CBR, PFS, TTR
- By investigator: ORR
- OS, safety, PK, immunogenicity

Demographic characteristics	Dato-DXd (N=137)
Median age (range), years	60 (29-79)
Female, n (%)	83 (61)
Histology, n (%)	
Adenocarcinoma	130 (95)
History of brain metastasis, n (%)[a]	70 (51)
Median prior lines of therapy for adv/met disease	3
Prior lines of therapy, n (%)	137 (100)
≥3 prior lines of therapy for adv/met disease	98 (72)
Prior platinum chemotherapy	137 (100)
Prior anti–PD-1/anti–PD-L1 immunotherapy	49 (36)
≥2 prior lines of targeted therapies for indicated genomic alteration	82 (60)



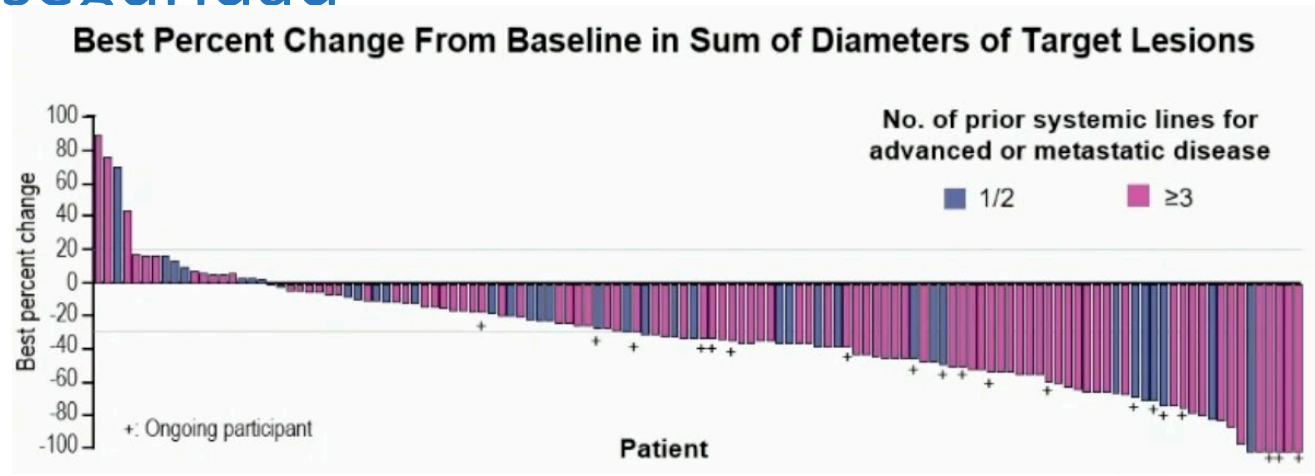
2ª línea en pacientes EGFRm. Progresión a osimertinib

TROPION-Lung 05: Eficacia y seguridad

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib



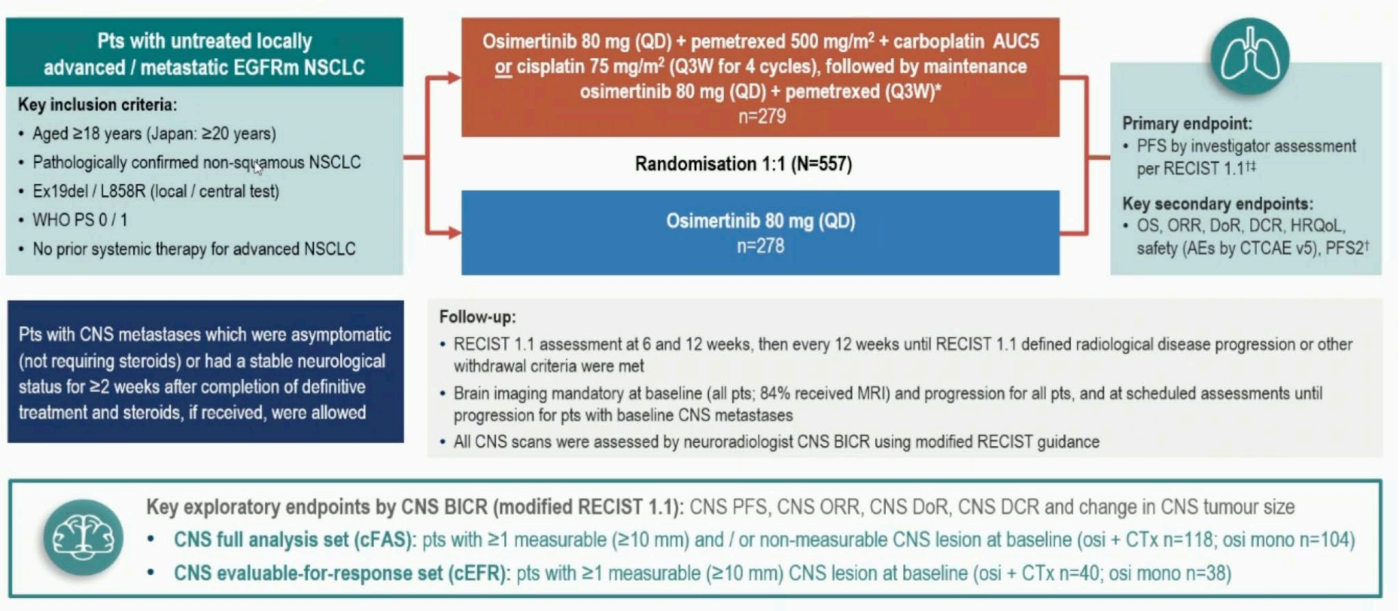
22% dose reduction, 10% withdrawal, 2% death

AESI Incidence by Grade[d]

n (%)	Total	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis	90 (66)	45 (33)	30 (22)	15 (11)
Ocular surface toxicity[e]	36 (26)	26 (19)	7 (5)	3 (2)[f]
IRR	22 (16)	15 (11)	7 (5)	0
Adjudicated drug-related ILD	5 (4)	1 (1)	3 (2)	1 (1)[g]

EGFR – Poblaciones especiales: MTS SNC

FLAURA 2: Fase 3



EGFR – Poblaciones especiales: MTS SNC

FLAURA 2: Fase 3

Pts with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:
- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles), followed by maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)*
n=279

Randomisation 1:1 (N=557)

Osimertinib 80 mg (QD)
n=278

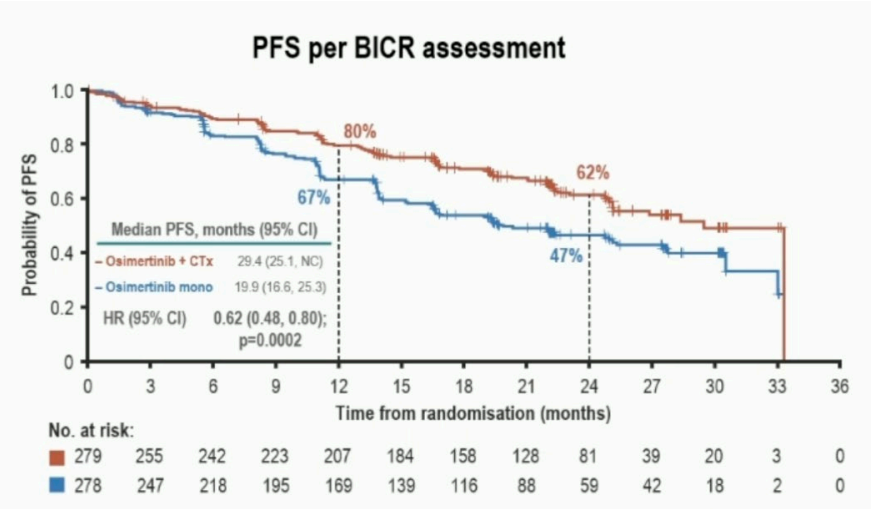
Primary endpoint:
- PFS by investigator assessment per RECIST 1.1†‡

Key secondary endpoints:
- OS, ORR, DoR, DCR, HRQoL, safety (AEs by CTCAE v5), PFS2†

Pts with CNS metastases which were asymptomatic (not requiring steroids) or had a stable neurological status for ≥2 weeks after completion of definitive treatment and steroids, if received, were allowed

Follow-up:
- RECIST 1.1 assessment at 6 and 12 weeks, then every 12 weeks until RECIST 1.1 defined radiological disease progression or other withdrawal criteria were met
- Brain imaging mandatory at baseline (all pts; 84% received MRI) and progression for all pts, and at scheduled assessments until progression for pts with baseline CNS metastases
- All CNS scans were assessed by neuroradiologist CNS BICR using modified RECIST guidance

Key exploratory endpoints by CNS BICR (modified RECIST 1.1): CNS PFS, CNS ORR, CNS DoR, CNS DCR and change in CNS tumour size
- **CNS full analysis set (cFAS):** pts with ≥1 measurable (≥10 mm) and / or non-measurable CNS lesion at baseline (osi + CTx n=118; osi mono n=104)
- **CNS evaluable-for-response set (cEFR):** pts with ≥1 measurable (≥10 mm) CNS lesion at baseline (osi + CTx n=40; osi mono n=38)



EGFR – Poblaciones especiales: MTS SNC

Iniciativa científica de: GECP

FLAURA 2: Fase 3

Pts with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles), followed by maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)*
n=279

Randomisation 1:1 (N=557)

Osimertinib 80 mg (QD)
n=278

Primary
- PFS
per R

Key se
- OS,
safety

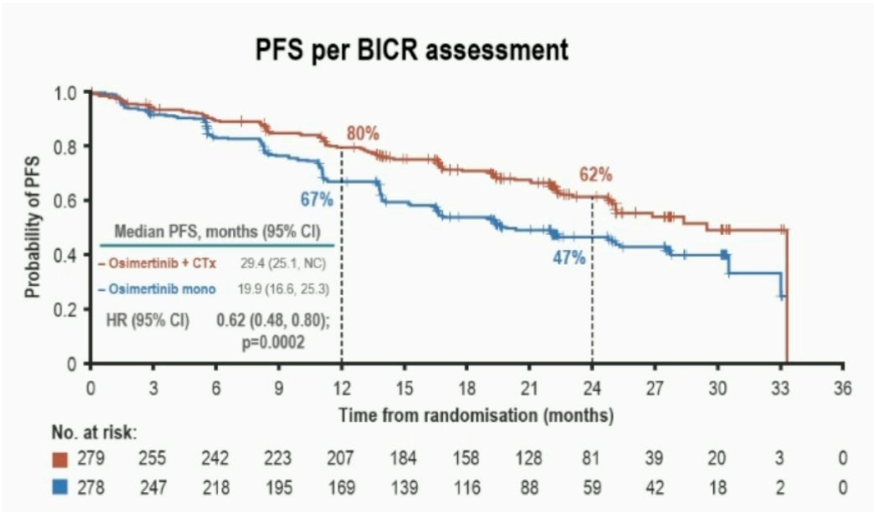
Pts with CNS metastases which were asymptomatic (not requiring steroids) or had a stable neurological status for ≥2 weeks after completion of definitive treatment and steroids, if received, were allowed

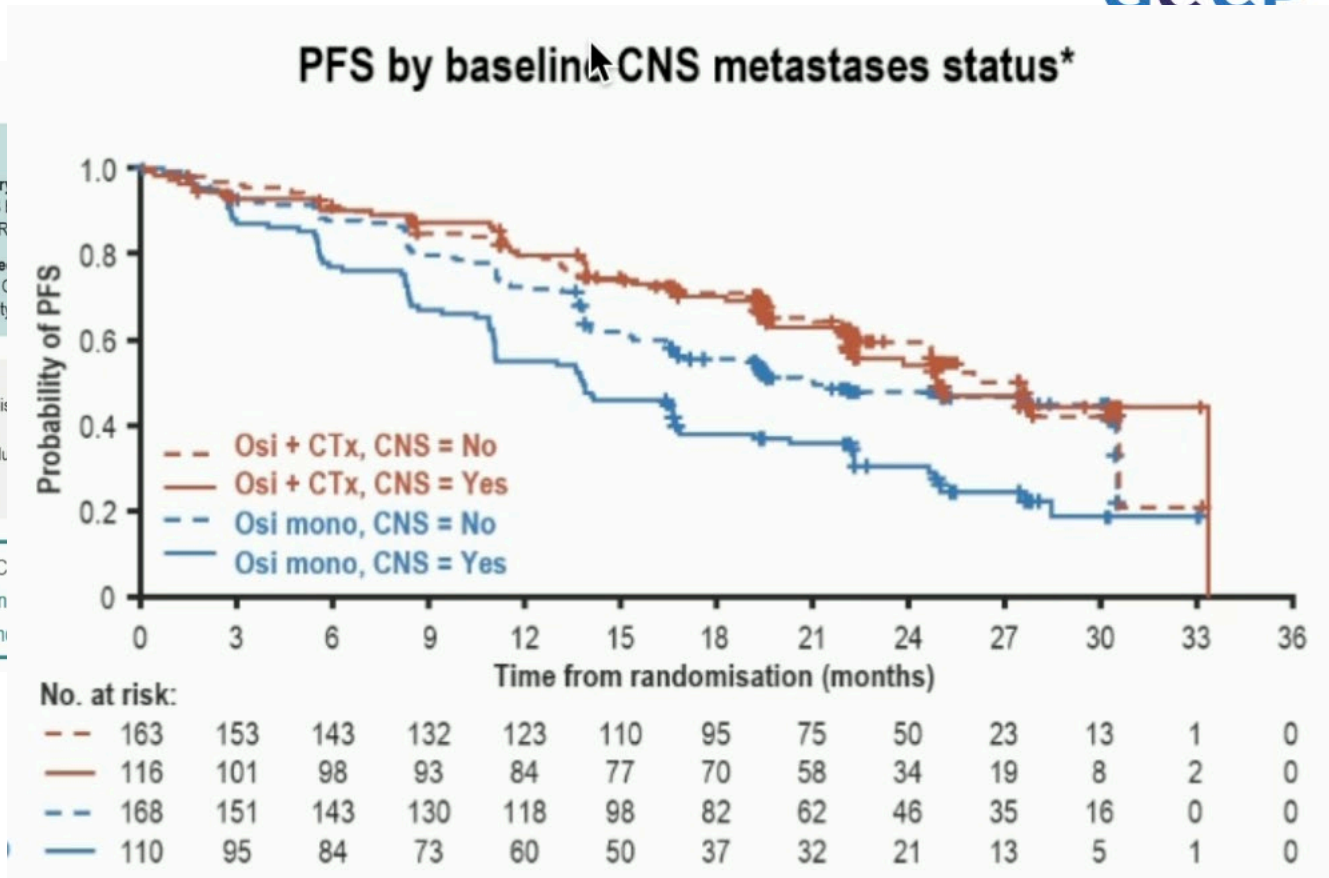
Follow-up:

- RECIST 1.1 assessment at 6 and 12 weeks, then every 12 weeks until RECIST 1.1 defined radiological dis withdrawal criteria were met
- Brain imaging mandatory at baseline (all pts; 84% received MRI) and progression for all pts, and at schedu progression for pts with baseline CNS metastases
- All CNS scans were assessed by neuroradiologist CNS BICR using modified RECIST guidance

Key exploratory endpoints by CNS BICR (modified RECIST 1.1): CNS PFS, CNS ORR, CNS DoR, CNS DCR and change in C

- **CNS full analysis set (cFAS):** pts with ≥1 measurable (≥10 mm) and / or non-measurable CNS lesion at baseline (osi + CTx n
- **CNS evaluable-for-response set (cEFR):** pts with ≥1 measurable (≥10 mm) CNS lesion at baseline (osi + CTx n=40; osi mon





EGFR – Poblaciones especiales: MTS SNC

FLAURA 2: Fase 3

Pts with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles), followed by maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)*
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Randomisation 1:1 (N=557)

Osimertinib 80 mg (QD)
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Primary
- PFS
per R

Key se
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safety

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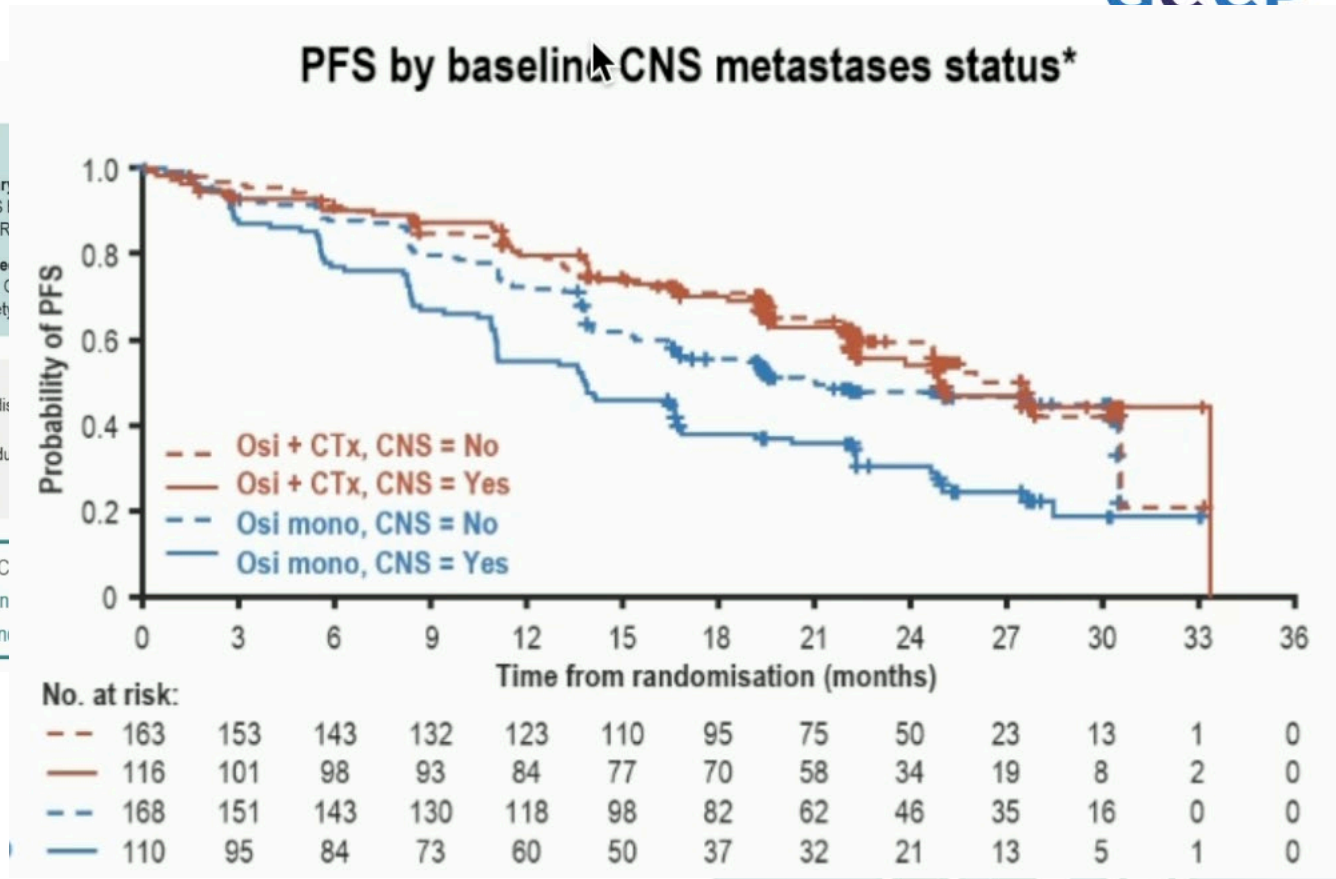


	cFAS (n=222) Measurable + non-measurable BM		cEFR (n=78) Measurable BM	
CNS response‡	**Osi + CTx (n=118)**	**Osi mono (n=104)**	**Osi + CTx (n=40)**	**Osi mono (n=38)**
CNS ORR, % (95% CI)	**73 (64 to 81)**	**69 (59 to 78)**	**88 (73 to 96)**	**87 (72 to 96)**
Complete response, n (%)	70 (59)	45 (43)	19 (48)	6 (16)
Partial response, n (%)	16 (14)	27 (26)	16 (40)	27 (71)
CNS DCR, % (95% CI)	91 (84 to 95)	93 (87 to 97)	95 (83 to 99)	97 (86 to 100)
Median DoR, months (95% CI)§	**NR (23.8, NC)**	**26.2 (19.4, NC)**	**NR (21.6, NC)**	**20.9 (12.6, NC)**

EGFR ex20

PAPILLON

Amivantamab Plus Chemotherapy vs Chemotherapy as First-line Treatment in *EGFR* Exon 20 Insertion–mutated Advanced Non-small Cell Lung Cancer (NSCLC)

Primary Results From PAPILLON, a Randomized Phase 3 Global Study

Nicolas Girard,[1] Keunchil Park,[2,*] Ke-Jing Tang,[3] Byoung Chul Cho,[4] Luis Paz-Ares,[5] Susanna Cheng,[6] Satoru Kitazono,[7] Muthukkumaran Thiagarajan,[8] Jonathan W. Goldman,[9] Joshua K. Sabari,[10] Rachel E. Sanborn,[11] Aaron S. Mansfield,[1] Jen-Yu Hung,[13] Sanjay Popat,[14] Josiane Mourão,[15] Archan Bhattacharya,[16] Trishala Agrawal,[17] S. Martin Shreeve,[18] Roland E. Knoblauch,[17] Caicun Zhou[19]

Iniciativa científica de: GECP lung cancer research

Study Design

Key Eligibility Criteria

- Treatment-naïve,[a] locally advanced or metastatic NSCLC
- Documented *EGFR* Exon 20 insertion mutations
- ECOG PS 0 or 1

Stratification Factors

- ECOG PS
- History of brain metastases[b]
- Prior EGFR TKI use[a]

1:1 Randomization (N=308)

- **Amivantamab-Chemotherapy** (n=153)
- **Chemotherapy** (n=155)

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at week 7 (first day of cycle 3)

Chemotherapy on the first day of each cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m^2 until disease progression

Primary endpoint: Progression-free survival (PFS) by BICR according to RECIST v1.1[c]

Secondary endpoints:

- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- PFS after first subsequent therapy (PFS2)
- Symptomatic PFS[d]
- Time to subsequent therapy[d]
- Safety

Optional crossover to 2nd-line amivantamab monotherapy[e]

Demographics

Characteristic, n (%)	Amivantamab-Chemotherapy (n=153)	Chemotherapy (n=155)
Median age, years (range)	61 (27–86)	62 (30–92)
Female / male	85 (56) / 68 (44)	93 (60) / 62 (40)
Race[a]		
Asian	97 (64)	89 (59)
White	49 (32)	60 (39)
Other[b]	5 (3)	3 (2)
ECOG PS 0 / 1	54 (35) / 99 (65)	55 (35) / 100 (65)
History of smoking: yes / no	65 (42) / 88 (58)	64 (41) / 91 (59)
History of brain metastases: yes / no	35 (23) / 118 (77)	36 (23) / 119 (77)
Prior EGFR TKI use: yes[c] / no	1 (1) / 152 (99)	3 (2) / 152 (98)
Histology: adenocarcinoma subtype / other[d]	151 (99) / 2 (1)	153 (99) / 2 (1)

At the time of the analysis:

- 70 p (46%) ongoing vs 24 p (15%)

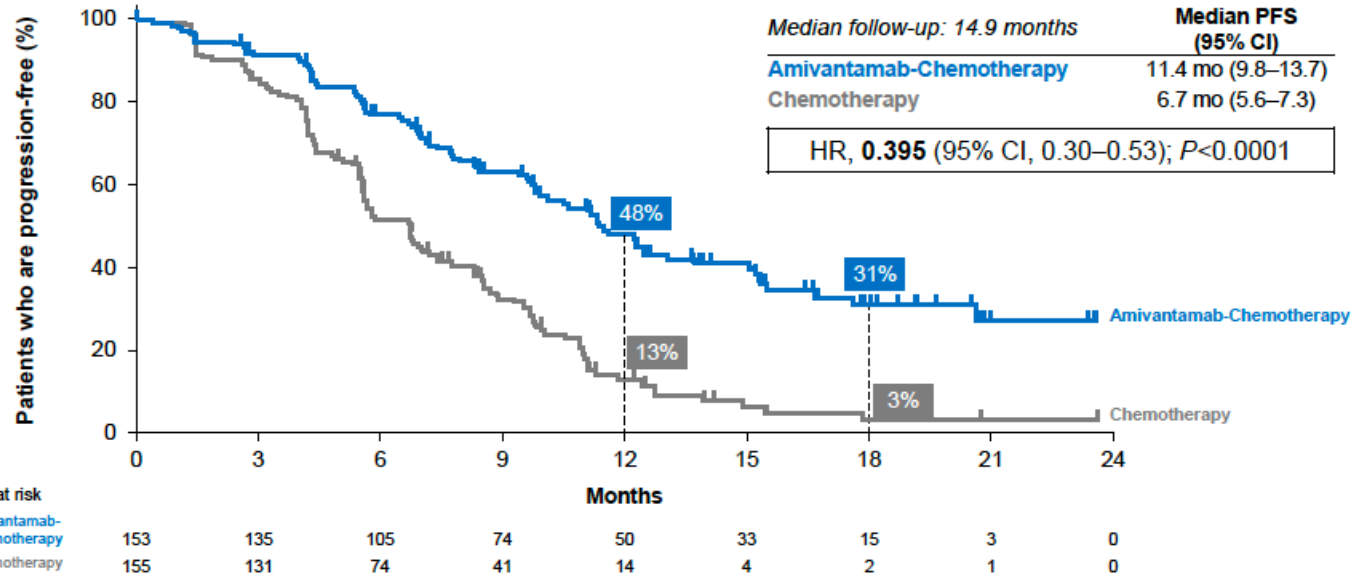
Discontinuation

- PD 50 p (33%) vs 107 p (69%)
- AEs 14 p (9%) vs 14 p (9%)

EGFR ex20

PAPILLON: Eficacia

Primary Endpoint: PFS by BICR



Median follow-up: 14.9 months	Median PFS (95% CI)
Amivantamab-Chemotherapy	11.4 mo (9.8–13.7)
Chemotherapy	6.7 mo (5.6–7.3)

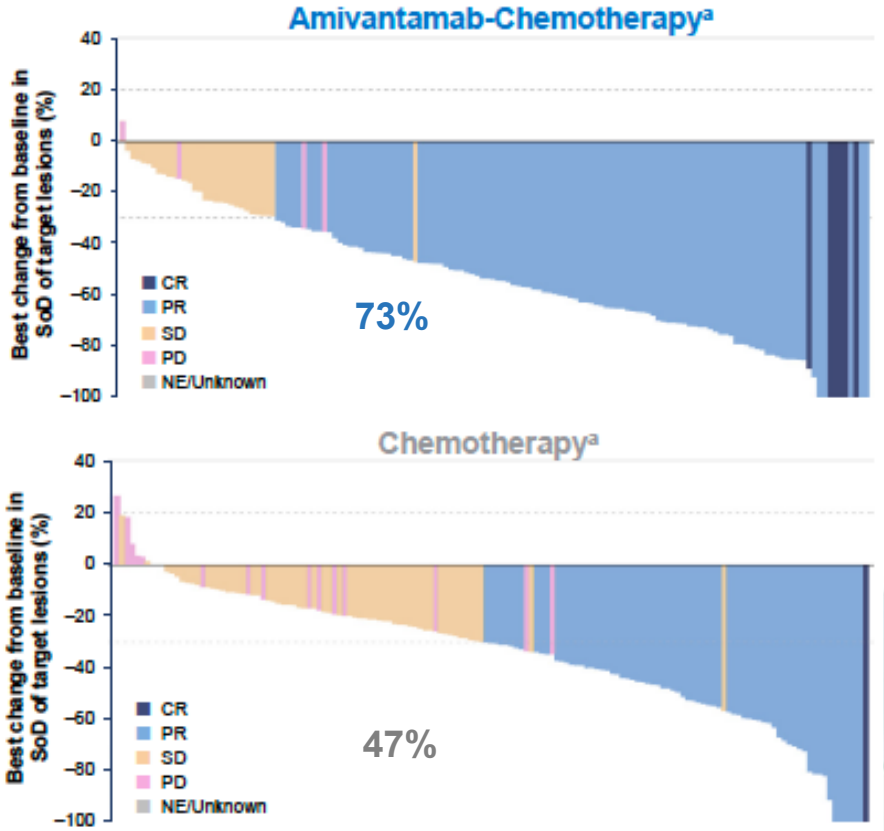
HR, **0.395** (95% CI, 0.30–0.53); *P*<0.0001

Median PFS2

	Median PFS2 (95% CI)
Amivantamab-Chemotherapy	NE (22.8–NE)
Chemotherapy	17.2 mo (14.0–21.5)

HR, **0.493** (95% CI, 0.32–0.76); *P*=0.001[b]

ORR



DoR 9.7 vs 4.4 m

EGFR ex20

PAPILLON: Efectos adversos

Iniciativa científica de: GECP lung cancer research

	Amivantamab-Chemotherapy (n=151)	Chemotherapy (n=155)
Median treatment duration, months (range)	9.7 (0.1–26.9)	6.7 (0–25.3)
No. of chemotherapy cycles, median (range)		
Carboplatin	4 (1–4)	4 (1–5)
Pemetrexed	13 (1–34)	10 (1–37)

Treatment-emergent AEs, n (%)	Amivantamab-Chemotherapy (n=151)	Chemotherapy (n=155)
Any AEs	151 (100)	152 (98)
Grade ≥3 AEs	114 (75)	83 (54)
Serious AEs	56 (37)	48 (31)
AEs leading to death	7 (5)	4 (3)
Any AE leading to treatment:		
Interruptions of any agent	104 (69)	56 (36)
Related interruptions of amivantamab	63 (42)	–
Reductions of any agent	73 (48)	35 (23)
Related reductions of amivantamab	54 (36)	–
Discontinuations of any agent	36 (24)	16 (10)
Related discontinuations of amivantamab	10 (7)	–
Discontinuations of all study agents due to AEs	12 (8)	12 (8)

Most common AEs of any cause by preferred term (≥20%), n (%)	Amivantamab-Chemotherapy (n=151)		Chemotherapy (n=155)	
	All grades	Grade ≥3	All grades	Grade ≥3
Associated with EGFR inhibition				
Paronychia	85 (56)	10 (7)	0	0
Rash	81 (54)	17 (11)	12 (8)	0
Dermatitis acneiform	47 (31)	6 (4)	5 (3)	0
Stomatitis	38 (25)	2 (1)	9 (6)	0
Diarrhea	31 (21)	5 (3)	20 (13)	2 (1)
Associated with MET inhibition				
Hypoalbuminemia	62 (41)	6 (4)	15 (10)	0
Peripheral edema	45 (30)	2 (1)	16 (10)	0
Other				
Neutropenia	89 (59)	50 (33)	70 (45)	35 (23)
Anemia	76 (50)	16 (11)	85 (55)	19 (12)
Infusion-related reaction	63 (42)	2 (1)	2 (1)	0
Constipation	60 (40)	0	47 (30)	1 (1)
Leukopenia	57 (38)	17 (11)	50 (32)	5 (3)
Nausea	55 (36)	1 (1)	65 (42)	0
Thrombocytopenia	55 (36)	15 (10)	46 (30)	16 (10)
Decreased appetite	54 (36)	4 (3)	43 (28)	2 (1)
Alanine aminotransferase increased	50 (33)	6 (4)	56 (36)	2 (1)
Aspartate aminotransferase increased	47 (31)	1 (1)	51 (33)	1 (1)
COVID-19	36 (24)	3 (2)	21 (14)	1 (1)
Hypokalemia	32 (21)	13 (9)	13 (8)	2 (1)
Vomiting	32 (21)	5 (3)	29 (19)	1 (1)

Neumonitis 3% en Ami+ChT

EGFR – Poblaciones especiales: Mutaciones no comunes

Iniciativa científica de: GECP

ARCHILLES/TORG1834: Fase 3

Study design ~ACHILLES/TORG1834~

Key inclusion criteria

Locally advanced/metastatic Non-Sq NSCLC
≥20 years
ECOG performance status 0 / 1
Sensitizing uncommon mutation*
No prior systemic anticancer /EGFR-TKI therapy
Stable CNS metastases allowed

Stratification factors
Mutation status (Single vs Compound)
Stage (III/IV vs Recurrence)
CNS metastasis (Yes vs No)
Afatinib dose (30 mg vs 40 mg)

R 109

1 → **Platinum + Pemetrexed ** Until PD (n=36)**

2 → **Afatinib 40mg or 30mg *** Until PD (n=73)**

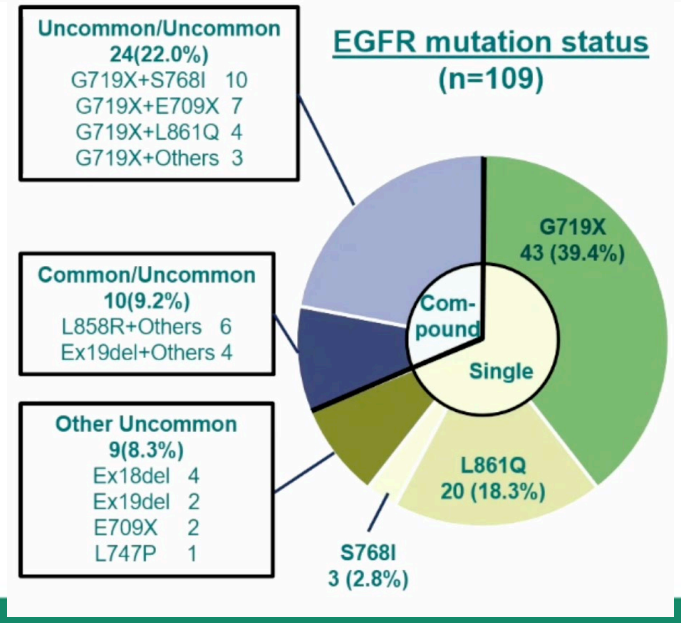
Clinical trial information: jRCTs031180175

* Uncommon/Compound EGFR mutations without exon 20 insertions and de-novo T790M mutations

** Cisplatin 75 mg/m² or carboplatin (AUC 5 or 6) and pemetrexed (500 mg/m²), followed by pemetrexed maintenance therapy every 3 weeks.

*** A 30 mg dose of afatinib could be selected for elderly/frail patients as a starting dose before randomization

Primary endpoint: Progression free survival (PFS) assessed by investigators



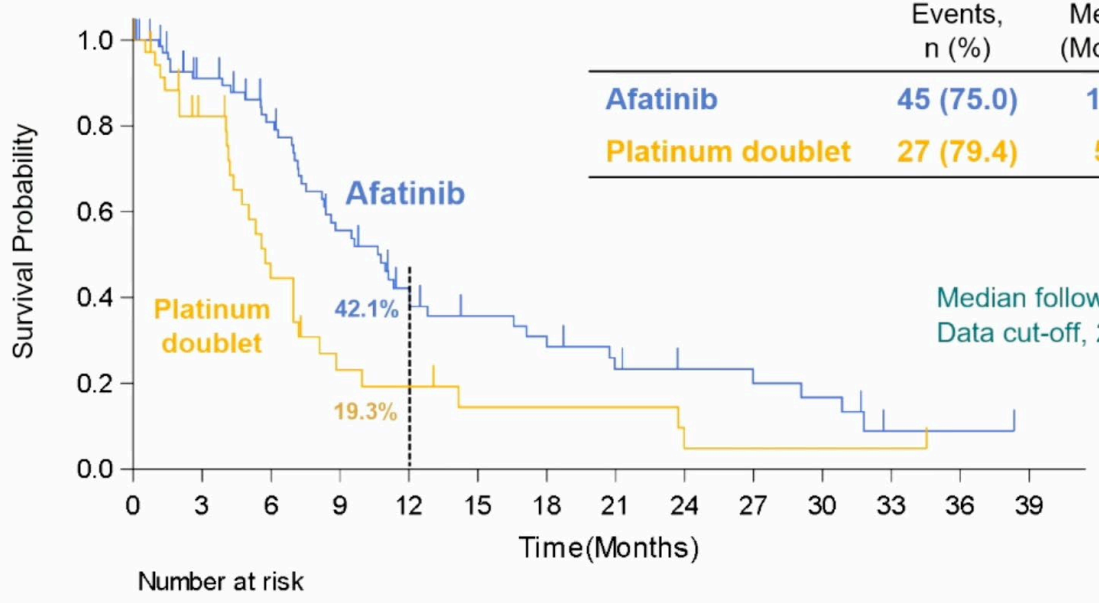
Characteristics		Afatinib (n=73)		Platinum Doublet (n=36)	
Age	Median (range)	71.0	(49-83)	66.5	(42-77)
	≥ 75 years old	19	(26.0%)	5	(13.9%)
Gender	Male	32	(43.8%)	16	(44.4%)
	Female	41	(56.2%)	20	(55.6%)
ECOG performance status	0	32	(43.8%)	16	(44.4%)
	1	41	(56.2%)	20	(55.6%)
Smoking status	Never	38	(52.1%)	13	(36.2%)
	Current	8	(11.0%)	6	(16.7%)
	Former	27	(37.0%)	17	(47.2%)
Stage*	III/IV	55	(75.3%)	29	(80.6%)
	Recurrence	18	(24.7%)	7	(19.4%)
EGFR mutation status*	Single	50	(68.5%)	25	(69.4%)
	Compound	23	(31.5%)	11	(30.6%)
CNS metastasis*	No	50	(68.5%)	25	(69.4%)
	Yes	23	(31.5%)	11	(30.6%)
Afatinib starting dose*	30 mg	37	(50.7%)	19	(52.8%)
	40 mg	36	(49.3%)	17	(47.2%)

EGFR - Poblaciones especiales: Mutaciones no comunes

ARCHILLES/TORG1834: Fase 3

Iniciativa científica de: GECP lung cancer research

Primary endpoint: Progression-Free Survival



	Events, n (%)	Median (Months)	HR (95% CI)	*p* value
Afatinib	45 (75.0)	10.6	0.422 (0.256-0.694)	0.0007
Platinum doublet	27 (79.4)	5.7		

*Efficacy boundary, p=0.0304

Median follow-up: 12.5 months (range, 0–43.5)
Data cut-off, 28 Feb 2023

HR: Hazard ratio

ORR

Afatinib 43 (61.4%)

ChT 16 (47.1%)

p=0.2069

Mensajes

- MARIPOSA: Ami + Lazertinib en pacientes EGFR+ en 1ª línea
  - Mejor mPFS
  - Mayor toxicidad
- MARIPOSA 2: Ami +ChT
  - Mejor mPFS
  - Mayor toxicidad (mayor si Lazertinib)
- TROPION-Lung 05: Datopotanab Deruxtecan
  - Buena actividad a la progresión a Osimertininb
- FLAURA 2: MTS SNC Osi + Cht 1L
  - Major eficacia que osimertinib
- PAPILLON: Ami + ChT beneficio en PFS, ORR, DoR en 1L ex20
- Afatinib superior a quimioterapia en mutaciones no comunes

Iniciativa científica de:

GECP lung cancer research